

PHOTOXYGENATION OF 7-SUBSTITUTED CYCLOHEPTATRIENES

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Abstract — Photoxygennation of 7-substituted cycloheptatrienes, including the Me, Et, iPr, Ph, CN, COOMe, COOEt, and CONH₂ groups was studied, and several products among the tropilidene-type (1 and 2) and norcaradiene-type (3 and 4) endoperoxides, o-substituted benzaldehydes (5), diepoxides (6 and 7), and ketoalcohols (8) were obtained. Mechanism of the formations of the products was discussed. Thermal isomerization of the endoperoxides (1, 3 and 4) to the corresponding diepoxides (10, 6 and 7), and the reaction of the endoperoxides (1 and 3) with triethylamine were examined.

Kende and Chu had reported evidence that the oxygenation of cycloheptatriene (tropilidene) by photochemically generated singlet oxygen gave [4 + 2] and [6 + 2] adducts by isolating their hydrogenation products.¹⁾ Recently, the extensive investigations of the oxygenation of tropilidene were independently carried out by Adam et al.,²⁾ Mori and Takeshita³⁾ and by us,⁴⁾ and various endoperoxides and their rearranged products were isolated and characterized. Furthermore, Ritter et al. studied the photoxygennation of methyl 7-tropylcarboxylate,⁵⁾ and Adam et al. described the photoxygennation of 7-substituted tropilidenes, including the CN, COOMe, CHO, OMe, and Ph groups, and mechanistic implications were discussed on the basis of theoretical and kinetic grounds.⁶⁾ We also reported the reaction of 7-, 1-, and 3-methoxytropilidenes for the purpose of isolation of oxygenation products and transformation to tropone derivatives.⁷⁾

We have investigated the photoxygennation of 7-substituted tropilidenes, including (a) Me, (b) Et, (c) iPr, (d) Ph, (e) CN, (f) COOMe, (g) COOEt, and (h)

CONH_2 groups. We obtained new type products, characterized including stereochemistry, and discussed the reaction mechanism especially on the stereochemical control of the reaction of tropilidene-norcaradiene equilibrium with oxygen. Furthermore, some transformations of endoperoxides were examined. These results will be reported in this paper.

The photooxygenation of 7-substituted tropilidenes was performed in the similar method to tropilidene itself in acetone in the presence of hematoporphyrin as sensitizer.^{4,7)} Several products among tropilidene-type [4 + 2] adducts (1; endo and 2; exo), norcaradiene-type [4 + 2] adducts (3; exo and 4; endo), α -substituted benzaldehydes (5), diepoxides (6 and 7), and ketoalcohols (8) were obtained after purification by column chromatography. The isolated yields are shown in Table 1.

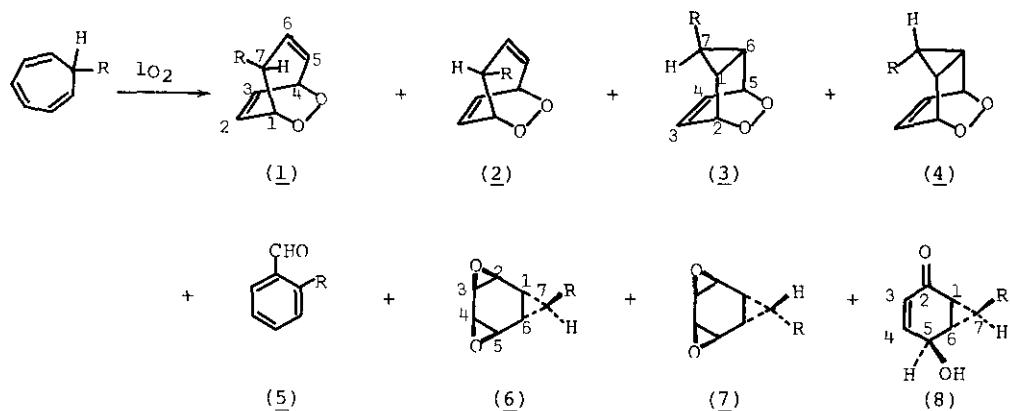


Table 1. Yields (%) of Photooxygenation Products of Tropilidenes.

| R | <u>1</u> | <u>2</u> | <u>3</u> | <u>4</u> | <u>5</u> | <u>6</u> | <u>7</u> | <u>8</u> |
|---|----------|----------|----------|----------|----------|----------|----------|----------|
| a; Me | 12.6 | 23.4 | 3.8 | - | 14 | - | - | - |
| b; Et | 36.1 | - | 7.0 | - | 7.5 | - | - | - |
| c; iPr | 22.6 | - | 33.9 | - | 4.2 | 5.4 | - | 22.5 |
| d; Ph | 8.2 | - | 60.1 | - | 3 | 3.3 | - | 12.4 |
| e; CN | - | - | 28 | 24 | 3 | 2 | 20 | - |
| f; COOMe | - | - | 60 | - | 10 | 18 | - | - |
| g; COOEt | - | - | 70 | - | 6 | 8 | - | - |
| h; CONH_2 (OMe) ⁷⁾ | - | - | 66 | - | - | - | - | - |
| | 40-50 | - | - | - | 5 | - | - | - |

The structures were assigned by extensive $^1\text{H-nmr}$ experiments including decoupling techniques and use of shift reagent. The melting points and $^1\text{H-nmr}$ data of the products and transformation products are shown in Table 2.

Benzaldehydes (5) were identified by direct comparison with authentic samples or by derivation to the corresponding benzoic acids. The compounds (6 and 7) were obtained by thermal isomerization of the corresponding endoperoxides (3 and 4), and ketoalcohols (8) were also obtained from 3 by treatment with triethylamine, the results will be described later. The compounds (6e and 7e) have established by X-ray analysis.⁸⁾

Although Adam et al. mentioned⁶⁾ that they obtained 2d and 2 ($R = OMe$) from 7-phenyl- and 7-methoxytropilidenes, respectively, as tropilidene-type adducts, we obtained endo isomers 1d and 1 ($R = Me$)⁷⁾, as sole tropilidene-type adducts.

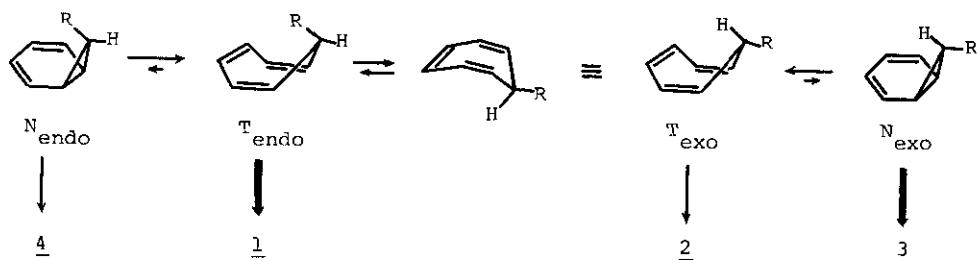
In the photooxygenation of 7-methyltropilidene, two stereoisomeric tropilidene type adducts (1a and 2a) were obtained. The stereochemistries were determined by using shift reagent. The nmr patterns of 1b and 1c were quite similar to those of 1a rather than 2a, which indicated their endo configuration. Furthermore, the ratio (0.9) of the shift value of 7-exo-H and that of 1-H (7-exo-H/1-H) in 1a in the presence of $Eu(fod)_3$ is almost twice of the value (0.5) of 7-endo-H/1-H in 2a. The similar values of 7-H/1-H of 1c (0.8) and 1d (0.8) to that of 1a were observed.

Stereochemistries of norcaradiene-type endoperoxides (3 and 4) were easily assigned by the characteristic coupling constants, $J_{1,7}$; larger value (ca. 7 Hz) was observed for endo isomer (4) than that (ca. 3 Hz) for exo isomer (3).⁶⁾

The product composition data (Table 1) qualitatively reveal that the norcaradiene-type adducts (3 and 4) increase at the expense of the tropilidene-type adducts (1 and 2) in the order (OMe) < Me < Et < iPr < Ph , being exclusively former for CN , $COOMe$, $CONH_2$ and exclusively latter for OMe .

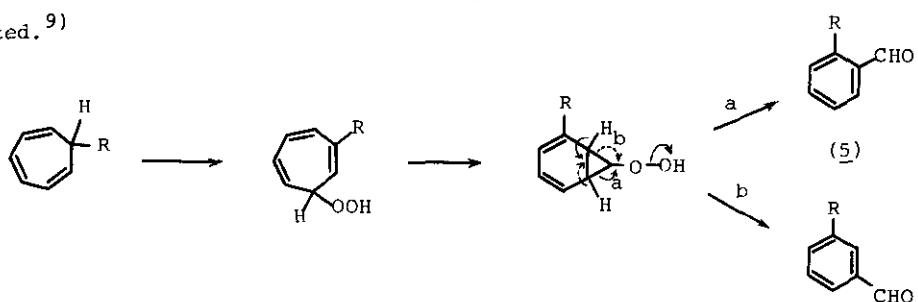
Adam beautifully explained the effect of π electron donating OMe and π electron accepting CN , CHO , $COOMe$ in the oxygenation of 7-substituted tropilidenes.⁶⁾ They discussed the reaction mechanism from the standpoints of (i) the electronic effect of the substituents on the stabilities of tropilidene and norcaradiene, and (ii) the comparison of activation energies of tropilidene-norcaradiene isomerization and of the reaction of these compounds with oxygen. They described that both of the tropilidene and norcaradiene adducts were derived from thermodynamically stable exo isomers. However, our results could not be rationalized merely by Adam's explanation.

The following mechanistic consideration will be proposed. 7-Substituted tropilidene can be considered to exist in the following equilibrium.⁶⁾ The adducts (1) were preferentially derived from T_{endo} which may be less stable conformer than



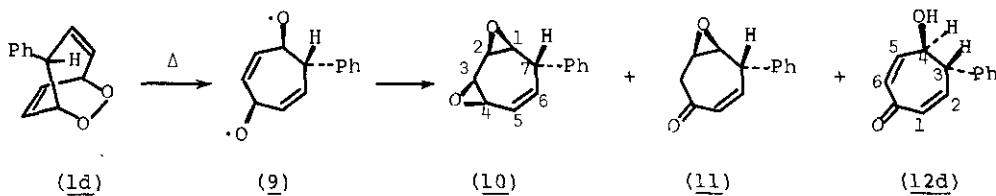
T_{exo} but is sterically less hindered in the reaction with oxygen. However, conformations T_{endo} and T_{exo} for the small methyl group are not as serious during approach of oxygen as for bulky isopropyl or phenyl group, and a mixture of endo and exo adducts was formed. On the other hand, norcaradiene-type adducts were preferentially derived from N_{exo} which may be more stable conformer than N_{endo} , but only tropilidene having the sterically small and linear cyano group gave a mixture of exo and endo isomers.

The formation of α -substituted benzaldehydes (5) may be explained by the following mechanism. However, another expected α -substituted isomer could not be isolated.⁹⁾



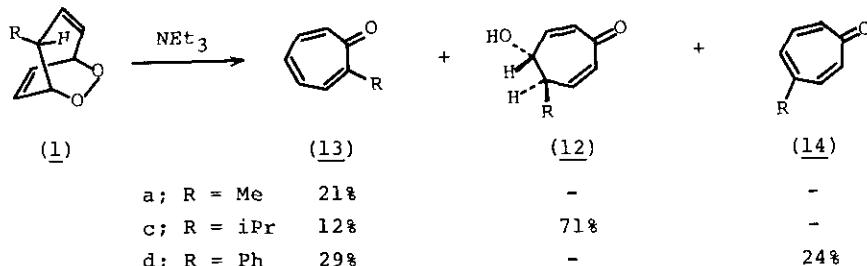
The formation of diepoxides (6 and 7) can be explained by photochemical transformation of (3 and 4) as observed in 3f⁵⁾ and ascaridol.¹⁰⁾ We suggest the mechanism of the formation of 8 by ionic cleavage of endoperoxides (3), although no catalyst was used in the reaction.

Similarly to previous reports,^{4,7)} the thermal treatment of 1d in boiling xylene was found to lead to three isomeric mixtures (10, 11, and 12d) in the yields of 23%, 7% and 26%, respectively. The compounds (10 and 11) must be formed from biradical (9), but 12 may be formed secondary from 10 and/or 11.



The similar thermal reaction of 3 and 4 in boiling xylene converted them into diepoxides (6 and 7), respectively, in good yields; 6c, 77%; 6d, 96%; 6e, 100%; 6g, 90%; 6h, 100%; 7e, 100%.

When endoperoxides (1) were treated with triethylamine, the corresponding tropones (13 and 14) and dihydrohydroxytropone (12) were formed, and dehydration of 12c,d with alumina afforded 4-substituted tropones (14c, 35%; 14d, 100%).¹¹⁾ 4-Isopropyltropone (14c) was identical with natural tropone, nezukone.



The treatment of 3 with triethylamine afforded ketoalcohols (8), whose oxidation with MnO_2 gave homo-p-quinone derivatives (15) in good yields.

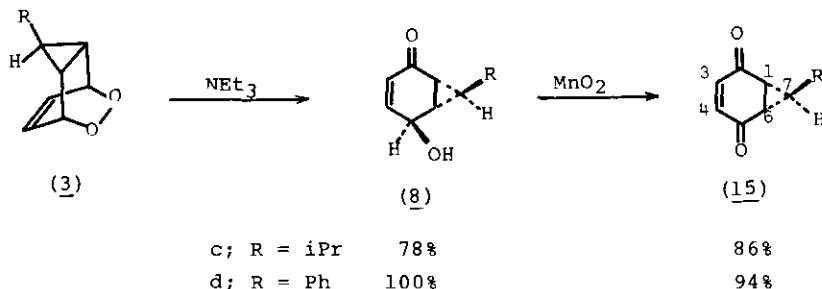


Table 2. Melting points and Nmr Spectral Data (δ ppm, J in Hz).

1a^a; oil; 0.95 (d, Me), 2.95 (m, H-7), 4.44 (dd, H-4), 4.58 (dd, H-1), 5.42 (dd, H-6), 5.99 (dd, H-5), 6.10 (ddd, H-2), 6.70 (ddd, H-3); $J(1,2=7.0, 1,3=1.0, 1,6=2.0, 1,7=5.0, 2,3=9.0, 2,4=1.5, 3,4=7.0, 4,5=7.0, 4,6=1.5, 5,6=10.5, 5,7=2.2, 6,7=3.0, 1,Me=7.0)$

1b^a; oil; 0.8-1.25 (m, Et), 2.81 (m, H-7), 4.44 (dd, H-4), 4.62 (dd, H-1), 5.46 (dm, H-6), 5.94 (dm, H-5), 6.09 (dm, H-2), 6.66 (dd, H-3); $J(1,2=6.0, 1,7=6.0, 2,3=9.0, 3,4=7.0, 4,5=7.0, 5,6=6.0)$

1c^b; oil; 0.96 (d, 2Me), 1.68 (m, 1H), 2.59 (m, H-7), 4.44 (dd, H-4), 4.73 (dd, H-1), 5.58 (dm, H-6), 6.03 (dd, H-5), 6.12 (dd, H-2), 6.65 (dd, H-3); $J(1,2=6.0, 1,3=1.2, 1,6=2.0, 1,7=6.0, 2,3=9.1, 2,4=1.3, 3,4=7.0, 3,5=0.5, 4,5=7.0, 4,6=1.1, 5,6=10.5, 5,7=2.2, 6,7=3.0)$

1d^b; mp 112-113°; 4.19 (m, H-7), 4.72 (ddm, H-4), 4.92 (ddm, H-1), 5.80 (dm, H-6), 5.93 (dm, H-2), 6.34 (ddd, H-5), 6.80 (ddd, H-3), 7.1-7.4 (Ph); $J(1,2=7.0, 1,3=1.0, 1,6=2.0, 1,7=5.0, 2,3=9.2, 2,4=1.2, 3,4=7.1, 3,5=0.5, 4,5=7.0, 4,6=1.0, 5,6=10.5, 5,7=2.4, 6,7=3.0)$

2a^a; oil; 1.26 (d, Me), 2.44 (m, H-7), 4.23 (d, H-1), 4.46 (dd, H-4), 5.45 (d, H-6), 5.89 (dd, H-5), 6.25 (dd, H-2), 6.63 (dd, H-3); $J(1,2=7.0, 1,3=1.0, 1,7=1.5, 2,3=9.0, 2,4=1.0, 3,4=7.0, 4,5=6.8, 4,6=1.0, 5,6=10.5, 5,7=2.2, 6,7=3.0, 7,Me=7.0)$

3a^a; oil; 0.3 (m, H-7), 0.95 (d, Me), 1.2 (m, H-1,6), 4.65 (ddd, H-2,5), 6.1 (dd, H-3,4); J(1,7=3.3, 2,3=4.2, 2,4=3.5, 7,Me=7.0)

3b^a; oil; 0.3 (m, H-7), 0.7-1.2 (m, H-1,6,Et), 4.7 (m, H-2,5), 6.18 (dd, H-3,4)

3c^b; mp 79-81°; 0.2 (dt, H-7), 0.9-1.2 (m, iPr), 1.25 (ddd, H-1,6), 4.71 (ddd, H-2,5), 6.13 (dd, H-3,4); J(1,2=3.3, 1,5=2.0, 1,7=3.3, 2,3=4.7, 2,4=3.5)

3d^b; mp 92-93° (94-96°)⁶; 1.50 (t, H-7), 1.90 (ddd, H-1,6), 4.95 (ddd, H-2,5), 6.38 (dd, H-3,4), 6.9-7.4 (Ph); J(1,2=3.2, 1,5=2.0, 1,7=3.0, 2,3=4.6, 2,4=3.5)

3e^b; mp 105-106° (107-108°)⁶; 0.99 (t, H-7), 2.28 (ddd, H-1,6), 5.00 (ddd, H-2,5), 6.30 (dd, H-3,4); J(1,2=3.2, 1,5=2.0, 1,7=3.2, 2,3=4.6, 2,4=3.3)

3f^b; mp 92-93° (95°)⁵ (93-95°)⁶; 1.21 (t, H-7), 2.21 (ddd, H-1,6), 3.67 (s, Me), 4.95 (ddd, H-2,5), 6.30 (dd, H-3,4); J(1,2=3.0, 1,5=2.0, 1,7=3.0, 2,3=4.5, 2,4=3.8)

3g^b; mp 76-77°; 1.22 (t, H-7), 1.24 (t, Me), 2.21 (ddd, H-1,6), 4.13 (q, CH₂), 4.96 (ddd, H-2,5), 6.31 (dd, H-3,4); J(1,2=3.0, 1,5=2.0, 1,7=3.0, 2,3=4.6, 2,4=3.8)

4e^b; mp 194-196° (194-195°)⁶; 1.50 (t, H-7), 2.15 (ddd, H-1,6), 5.13 (ddd, H-2,5), 6.50 (dd, H-3,4); J(1,2=3.7, 1,5=2.0, 1,7=7.0, 2,3=4.5, 2,4=3.5)

6c^b; mp 93.5-94°; 0.6-0.8 (m, H-7), 0.9-1.1 (m, iPr), 1.25 (bd, H-1,6), 3.20 (s, H-2,3,4,5); J(1,7=4.5)

6d^b; 147-148° (149-150°)⁶; 1.8-2.1 (m, H-1,6,7), 3.35 (s, H-2,3,4,5), 7.0-7.4 (Ph)

6e^b; mp 158-159° (159-160°)⁶; 1.52 (t, H-7), 2.15 (bd, H-1,6), 3.27 (bs, H-2,3,4,5); J(1,7=4.6)

6f^b; mp 113-114° (114-115°)⁶ (117)⁵; 1.75 (t, H-7), 2.08 (d, H-1,6), 3.30 (s, H-2,3,4,5), 3.75 (s, Me); J(1,7=4.4)

6g^b; mp 91-92°; 1.27 (t, Me), 1.74 (t, H-7), 2.07 (d, H-1,6), 3.26 (s, H-2,3,4,5), 4.15 (q, CH₂); J(1,7=4.4)

7e^b; mp 198-199° (199-200°)⁶; 1.88 (s, H-1,6,7), 3.35 (bs, H-2,5), 3.48 (bs, H-3,4)

8c; Acetate^a; mp 43.5-44.5°; 0.9-1.2 (m, H-7,iPr), 1.66 (m, H-1,6), 2.00 (COMe), 5.60 (bd, H-5), 5.84 (d, H-3), 6.45 (ddd, H-4); J(3,4=10.5, 4,5=5.0, 4,6=2.0)

8d^b; mp 145-146°; 2.2-2.6 (m, H-1,6,7), 2.8 (bs, OH), 4.61 (bd, H-5), 5.98 (d, H-3), 6.69 (ddd, H-4), 7.0-7.4 (Ph); J(3,4=10.5, 4,5=5.0, 4,6=2.0)

10^b; mp 74.5-75.5°; 2.93 (dd, H-1), 3.14 (dd, H-2), 3.42 (ddd, H-4), 3.59 (dd, H-3), 4.34 (ddd, H-7), 5.67 (ddd, H-5), 5.90 (ddd, H-6), 7.0-7.5 (Ph); J(1,2=4.0, 1,7=6.0, 2,3=2.0, 3,4=4.0, 4,5=3.5, 4,6=1.0, 5,6=11.2, 5,7=2.0, 6,7=5.0)

12d^b; oil; 1.87 (bs, OH), 3.98 (dt, H-3 or H-4), 4.79 (dt, H-4 or H-3), 6.13 (ddd, H-1 or H-6), 6.18 (ddd, H-6 or H-1), 6.56 (dd, H-2 or H-5), 6.66 (dd, H-5 or H-2), 7.0-7.3 (Ph); J(1,2=5,6=13.0, 2,3=4,5=2.5, 3,4=11.0, 1,3=1,6=4,6=2.3)

15c^b; mp 74-75.5°; 0.9-1.6 (m, iPr), 1.87 (dt, H-7), 2.40 (d, H-1,6), 6.39 (s, H-3,4); J(1,7=4.5)

15d^b; mp 127-129°; 2.87 (d, H-1,6), 3.10 (t, H-7), 6.49 (s, H-3,4), 7.0-7.4 (Ph); J(1,7=4.6)

a; in CCl₄. b; in CDCl₃.

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References and Notes

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